Center for Musculoskeletal Research

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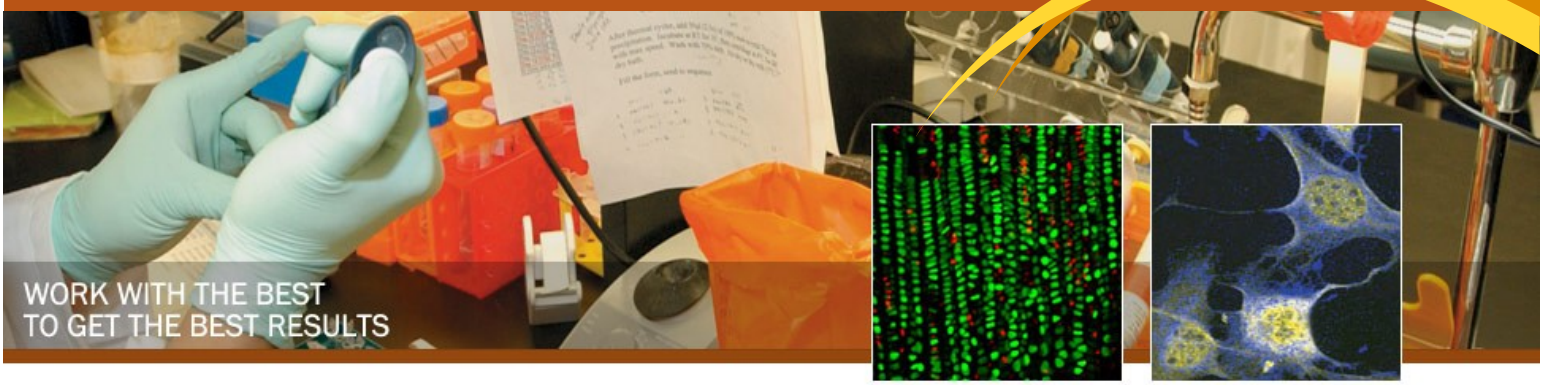
http://musculoskeletalcore.wustl.edu/home.aspx



Dr. Regis O'Keefe Visits Washington University Medical School

Dr. Regis O'Keefe is a national leader in the field of orthopaedics and musculoskeletal research. He is the Chair of the Department of Orthopaedics and Rehabilitation, and the Director of the Center for Musculoskeletal Research at the University of Rochester School of Medicine and Dentistry in Rochester, New York. Dr. O'Keefe is an orthopaedic oncologist, caring for patients with fragility fractures from osteoporosis, osteopenia, osteogenesis imperfect, and low vitamin D.

While visiting Washington University, Dr. O'Keefe gave a lecture entitled "Improving Orthopaedic Care Through Translational and Clinical Research: Opportunities and Challenges" the Arthur H. Stein, Jr. Lecture in the Department of Orthopaedic Surgery. He also gave the Louis V. Avioli Memorial Lecture entitled " Stem Cell Population and Their Regulation in Bone Repair."

Dr. Sandell, Dr. O'Keefe

Dr. O'Keefe is a member of the External Advisory Committee for the Center for Musculoskeletal Research here at Washington University Medical Center.

For more information on the Cores, please click on the links below:

Core A—Administrative Core
Core B—Structure and Strength Core
Core C—In Situ Molecular Analysis Core
Core D—Mouse Genetics Models Core

this issue

AVIOLI Musculoskeletal Seminar Series

Fridays @ 9am
Conf Rm 2 | CAM Building

May-June Schedule

5/06	**Clarissa Craft *(Mecham Lab)*** *Washington University*
5/13	**No Seminar**
5/20	**No Seminar**
5/27	**Keith Hruska** *Washington University*
6/03	**Kwadwo Oduro** *Washington University*
6/10	**Valarie Salazar** *Washington University*

WASHINGTON UNIVERSITY
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Remember to include reference to support from the Center in your abstracts and publications. Cite Grant # P30AR057235 from the National Institute Of Arthritis And Musculoskeletal And Skin Diseases.

Who's using our Cores?

Wei Zou, Ph.D *(Department of Pathology & Immunology)*

Osteoporosis is endemic in western society and is always caused by a relative increase in the activity of osteoclasts, the unique resorptive cells of bone. Our laboratory focuses on the molecular and cellular mechanisms by which osteoclasts form and degrade the skeleton with the goals of understanding the pathogenesis of osteoporosis and identifying potential therapeutic targets. With the help of **Core C**, we have determined the significance of the αvβ3 integrin and its outside-in activation induced signaling pathway including c-Src, Syk, ITAM proteins, the adptor SLP-76, the guanine nucleotide exchange factor, Vav3 and the Rho GTPases, Rac and cdc42.

Inside-out activation is an indirect process in which signals derived from an occupied receptor, typically that of a cytokine or growth factor, targets the intracellular domain of an integrin resulting in the conformation change of its external domain. The conformational change causes the integrin to bind its ligand with high affinity and transmit matrix-derived (outside-in) signals including those that organize the cytoskeleton.

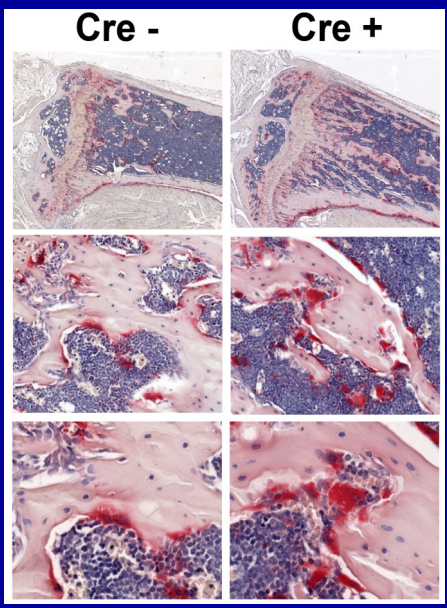
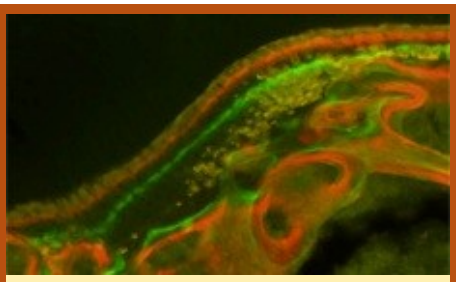


Figure 1: TRAP-stained histological sections of proximal tibia of 8 wk old control (-) and CtsK-*TLN1* (+) mice. (top panel 25X; middle panel 200X; lower panel 400X). It shows enhanced trabecular bone volume in the mutant mice, despite normal numbers of osteoclasts.

The interaction of talin1 with β-subunit cytoplasmic domains is an essential step in integrin activation. Therefore, we are using mice in which talin has been specifically removed in mature osteoclasts.

This project required preparation of numerous high quality, TRAP stained histological sections of bone as well as whole calvariae which was expertly performed by Core C. The core also generated non-decalcified sections for dynamic analysis of bone formation. We quantified these sections histomorphometrically using Core C microscope and image analysis system.



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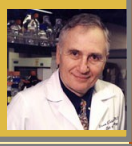

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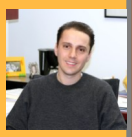

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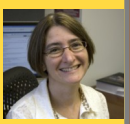

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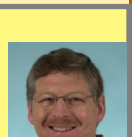

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